UNITED NATIONS WORLD HEALTH ORGANIZATION

EXPERT COMMITTEE ON VENEREAL INFECTIONS: REPORT ON THIRD SESSION

The third session of the Expert Committee on Venereal Infections was held from October 10 to 20, 1949, in Washington, D.C. The following members attended the meetings* : Dr. W. E. Coutts, Professor of Venereology, Chief, Department of Social Hygiene, Public Health Administration, Santiago, Chile ; Dr. R. Degos, Associate Professor of the Faculty of Medicine and "Médecin des Hôpitaux de Paris", Paris, France ; Dr. S. Hellerstrom, Professor of Dermato-syphilology, University of Stockholm, Stockholm, Sweden ; Dr. E. H. Hermans, Medical Director, Venereal Diseases, Rotterdam, Holland ; Dr. J. F. Mahoney (chairman), Chief of Laboratory of Antibiotic Research and Development, Section of Laboratory and Infectious Disease, Microbiological Institute, National Institute of Health, Staten Island, New York, U.S.A. ; Dr. G. L. M. McElligott (rapporteur), Director, Venereal Disease Department, St. Mary's Hospital, Venereal Disease Adviser, Ministry of Health, London, England ; Dr. Ibrahim Hanafi Nagi, Chief, Venereal Disease Division, Ministry of Public Health, Cairo, Egypt ; Dr. R. V. Rajam (vice-chairman), Professor of Venereology, Government General Hospital, Madras, India.

Consultants co-opted by the committee for technical advice on special items on the agenda were : Dr. Evan W. Thomas, Professor of Clinical Medicine, New York University College of Medicine, Consultant, United States Public Health Service, Director, Rapid Treatment Centre, Bellevue Hospital, New York, N.Y. ; Dr. Norman R. Ingraham, Institute for the Study of Venereal Diseases, University of Pennsylvania, Philadelphia, Penn., U.S.A. ; Dr. Poul V. Marcussen, Chairman, WHO Syphilis Study Commission to the United States, Copenhagen, Denmark.

Observers for the International Union against Venereal Diseases were : Mr. A. Woodchek, International Labour Office ; Dr. W. F. Snow, President, International Union against Venereal Diseases ; Dr. P. Sanchez, Chief, Venereal Disease Division, Department of Health, Caracas, Venezuela.

Dr. T. Guthe and Dr. A. Spillmann, of the Venereal Disease Section, WHO, represented the WHO Secretariat.

Dr. G. E. Samame, Venereal Disease Consultant, represented the Pan-American Sanitary Bureau.

By invitation of the chairman members of the sub-committee on Serology and Laboratory Aspects, and of the WHO Syphilis Study Commission to the U.S.A., attended several meetings. Dr. J. E. Moore, Chairman of the Venereal Disease Committee, National Research Council, U.S.A., Dr. T. Bauer, Chief, Venereal Disease Division, United States Public Health Service, and Dr. E. Gurney Clark, President, American Association of Venereal Disease, attended some of the meetings of the committee.

At its first meeting the committee elected Dr. J. F. Mahoney as chairman, Dr. R. V. Rajam as vice-chairman and Dr. G. L. M. McElligott as rapporteur. The committee considered the provisional agenda which was adopted with minor modifications.

Sub-Committee on Serology and Laboratory Aspects.—Special attention was paid to the committee's relationship to the sub-committee on Serology and Laboratory Aspects, which held its first session from October 12 to 20, 1949. In approving the agenda of the sub-committee, it was decided that Dr. P. Marcussen, co-opted consultant of the main committee, should act as liaison in matters of clinical syphilis. The terms of reference of the sub-committee, generally proposed by the previous two sessions of the main committee, and approved by the Executive Board and the World

* The following member of the committee was unable to attend : Dr. M. Grzybowski, Professor of Dermatology, Clinic of Dermatology, University of Warsaw, Poland.

Health Assembly, were more specifically defined as follows :

(1) To advise on matters relating to the organization of the International Serodiagnostic Laboratory Conference, approved by the Health Assembly, and to propose plans for this conference, including objectives, technical operation and timing ; and further

(2) To advise on other matters on the agenda, particularly the comparative treponematoses study proposed in the WHO Bejel project.

The committee considered its relationship to the WHO Syphilis Study Commission to the U.S.A. and noted the terms of reference of this commission. It was agreed that the preliminary statement of the commission to the Expert Committee be presented to the fifth session of the WHO Executive Board in January 1950, along with the report of the Expert Committee.

The committee noted the approval by the Executive Board of the *ad hoc* Expert Committee's report on its second session (October, 1948) and the observations made by the Board. The committee noted further the considerations of the Executive Board at its fourth session on the local implementation of the Brussels Agreement in the Rhine River Area.

In considering the maritime aspects of venereal-disease control generally, and the projected revision of the Brussels Agreement as part of future international health regulations for venereal-disease control, the committee established a working party* to study agenda items relating to this subject, and to report and make recommendations to the main committee.

The committee considered carefully the extensive documentation made available prior to and during the session, and relating to the development of the WHO venereal-disease programme, the present and the projected scope of the work, as well as other supporting documentation. Major emphasis was placed on technical orientation in the discussions, the programme elements and general outlook of WHO in the field of venereal-disease control having already been considered at the first and second sessions of the committee. Consideration of control techniques, the statement of the WHO Syphilis Study Commission to the U.S.A., antibiotic therapy in syphilis and related diseases, and serology and laboratory aspects (including the report of the sub-committee on Serology and Laboratory Aspects) took a major share of the committee's deliberations.

* *Members* : Dr. G. L. M. McElligott ; Dr. W. E. Coutts ; Dr. E. G. Hermans. *Consultants* : Dr. N. Jungalwalla ; Dr. T. I. Putkonen.

Developments and Perspectives

WHO Venereal-Disease Activities.—The development in each country of a venereal-disease control structure within the framework of the health administration, which will permit a maximum degree of control, should remain one of the aims of WHO. The larger reservoirs of syphilis and other venereal diseases are found in less developed areas where anti-venereal-disease activities have only been organized to a limited extent. A high priority should be given by WHO to assisting countries in such areas, and emphasis should continue to be placed on early syphilis of the sporadic or endemic type in the WHO venereal-disease programme in 1950 and 1951.

At the request of health administrations, WHO should continue to assist countries with advisory and demonstration services, and to stimulate the training of personnel for administrative, clinical, and laboratory work, without which a permanent control structure cannot be developed. In its assistance programme emphasis should be placed on teaching and training through support of national training institutions in regions where only limited facilities exist. Although requirements vary, the support of national training institutions by WHO by the provision of teaching equipment, supplies, and literature, as well as of temporary consultants, teaching staffs, and travelling seminars composed of highly specialized experts would accelerate the establishment of this programme, when co-ordinated with venereal-disease control training-courses under the WHO fellowship programme. Wherever possible, such training activities should develop into broader programmes for post-graduate work in public health and hygiene.

Any group of public health workers who attain a high degree of specialization may tend to overlook the fact that in the final analysis their work will prove productive only if supported by a genera programme of disease prevention. Isolated efforts directed towards specific problems will as a rule have difficulty in surviving unless integrated in an overall programme. In the present situation WHO forces devoted to venereal-disease control are in a position to enter the field with a minimum of preparation and to assist in the organization of control measures with a minimum of delay, financial outlay, and scientific personnel. The *entrée* thus effected by venereal-disease workers should be followed as soon as possible by the other equally important, but sometimes less flexible, public-health and sanitation activities. The committee is fully aware of the similar functions to be ascribed to "spearheads" represented by malaria, tuberculosis, and other specialized programmes, and that

similar developments into broader public-health programmes can well take place where these diseases are prevalent. There is no doubt, however, of the appeal of syphilis in pregnancy and congenital syphilis in all venereal-disease programmes. In co-operation with the forces devoted to the furthering of maternal and child health, the measures to be taken should be aimed at the identification of the disease in women, the provision of adequate therapy, and the postpartum observation of mother and child. In addition, the entry into the family units of the physician, nurse, health educator, or social worker permits scrutiny of the syphilitic status of the other family members and the taking of necessary steps to prevent reinfection. This approach may in some areas represent a basis for a wider understanding of the general epidemiological principles of case-finding and contact investigation in venereal-disease control. Wherever venereal-disease teams are assigned to work with health administrations in the field, pediatric personnel, health educators, etc., should be introduced as soon after the establishment of the venereal-disease activities as possible.

Another natural development would be the combination of anti-syphilis programmes with measures against other treponematoses, where these are prevalent. The general vulnerability of the causative agents of yaws, bejel, and pinta to penicillin attack has been projected elsewhere. Co-operative undertakings with tuberculosis, malaria, and other field units should be undertaken, wherever possible; when initial mass examinations offer administrative as well as public health advantages.

In areas where WHO field units are working with health administrations in demonstration areas, the operational centres and the laboratory facilities should be utilized as provisional training-centres under a plan (developed by the health administration and WHO) for the instruction of national trainees as well as personnel from other countries in the region.

Ultimately, the development in demonstration areas of the full complement of public health services would be a desideratum, a major effort being made to expand in such spearhead areas as have proved successful, and to maintain the broad gains obtained through the establishment of the activity under the leadership of the local or national health administration.

Active case-finding aiming at the identification and prevention of syphilis in pregnant women and infants represents an important stimulating element in organized large-scale, nation-wide venereal-disease control programmes, or broad maternal and child-health activities. The committee observes with satisfaction that this outlook (as originally recommended by the committee at its second session) has been the basis for the WHO/UNICEF participation in, and encouragement of, the anti-syphilis campaigns of the national health administrations in Bulgaria, Czechoslovakia, Finland, Hungary, Italy, Poland, and Yugoslavia. The development of these campaigns, the considerable activities of WHO technical consultants for programme discussion, inception, and follow up, the amount of medical literature and the number of fellowships granted by WHO, as well as the significant penicillin supplies and laboratory equipment furnished by UNICEF, are noted by the committee.

It is felt that the policy of stimulating governments to develop integrated health activities, so that programmes may continue to operate when outside assistance is withdrawn, is basically sound, and that programmes of this kind should go forward in countries where surveys have been, or are being, carried out, such as South-East Asia, the Middle East, and the Americas.

In many countries health administrations and national institutions have limited access to venereal-disease literature. Experience has shown that the time required for important contributions to appear in print and be distributed often represents an important delay in the acquisition of information on technical developments. With the very rapid technical development in the therapeutic and laboratory aspects of venereal-disease control (penicillin in syphilis, and cardiolipin-lecithin antigens in serodiagnosis) this situation is considered to be of some significance. WHO should, therefore, continue to assist health administrations and national institutions in this field. Corresponding members of the expert committee could assist in bringing major developments in each country to the attention of WHO.

In considering the long- and short-term objectives of WHO as set forth in the 1950 programme, the committee recommends that:

(1) WHO should proceed cautiously towards the long term objectives set forth in WHO Official Records, **18,** 86, and that priority be given to economically underdeveloped areas with a high prevalence of syphilis (and/or other treponematoses).

(2) The 1950 programme and outlook be the basis for the activities in 1951 and 1952 to enable consolidation of the gains obtained, development of polyvalent services in national programmes and in demonstration areas after initial venereal-disease operational activities, with particular emphasis on maternal and child health, and health education, being desirable.

(3) Emphasis be placed on assisting countries to establish in the health administrations at least a basic venereal-disease control structure headed by a health officer specializing in venereal-disease control.

(4) WHO should support selected venereal-disease-training activities in the regions where limited facilities are available, and regular training-courses be set up in training-institutions under an organized fellowship programme, preferably where such a programme can become part of an overall public-health educational system.

(5) WHO should encourage the establishment of venereal-disease literature units in health administrations and other suitable institutions, and continue to prepare and distribute to such units, under the WHO literature programme, venereal-disease literature, technical releases, and reference-lists on clinical, epidemiological, and other aspects of venereal-disease control.

(6) The Director-General should appoint further corresponding members in different countries and that these members make available to WHO and the expert committee, information on major technical developments in their respective countries.

International Health Regulations and Maritime Aspects of Venereal-Disease Control.–Following the post-war peak in 1946/47, the incidence of venereal disease, particularly early syphilis, declined significantly in some areas of the world, notably North America, Europe, and Australia. The extent of this fall has been less marked in seaports than in inland areas. An entirely different picture is seen in other regions of the world, and important foci of syphilis and gonorrhoea remain in many less developed areas, possibly on a larger scale than before. With an envisaged industrial development in these areas and further increase in maritime communications, the chances of introducing venereal infections to less prevalent areas are increased. In noting the unavoidable delays in the development of the international health regulations for venereal-disease control, the principles of which have been approved by the Health Assembly, the necessity is emphasized for interim measures in relation to the Brussels Agreement of 1924 relating to treatment facilities for seafarers. This agreement remains the sole practical instrument for venereal-disease control between countries. Among the present 56 signatories to the agreement, there are only 21 countries, twenty of which are members of WHO, the additional signatories being represented by individual island-groups, dependencies, or special ports.

The committee wishes to reiterate its previous statement concerning the importance of collecting basic data on venereal-disease morbidity. Notification by physicians as well as medical institutions to the health administration for statistical purposes should be adopted by countries as a routine procedure, at least as far as primary, secondary, and infantile congenital syphilis are concerned. Such data should be available also in regard to the nationality of cases thus recorded, so that the health administrations of maritime countries may obtain information on the possible reservoir of infection among their nationals outside the country in its maritime population.

Recognizing the interference by venereal diseases with the working capacity of maritime and industrial populations, the committee notes the special interest of the International Labour Organization and the International Union against Venereal Disease, and their co-operation with WHO, particularly in regard to the Rhine River project, which further emphasizes the need for international co-operative undertakings in this field.

While the introduction of almost immediate sterilizing therapy for gonorrhoea and syphilis, and the increasing application of ambulatory treatment based on repository penicillin preparations, may make it possible—depending upon the nature of each individual case—to retain seafarers and watermen aboard ship after initial treatment by a physician, there has, on the other hand, been an increasing tendency for treatment to be undertaken aboard ship by untrained personnel, without diagnosis. This practice is being encouraged by the carrying of authorized or non-authorized penicillin supplies for emergency or other purposes. This procedure is responsible for the loss of valuable epidemiological information and poor follow-up of the patient. Having studied the report of the working party set up to consider the question of international health regulations and maritime venereal-disease control, the committee recommends that :

(1) WHO draw the attention of governments to the desirability of more countries adhering to the International Agreement of Brussels whilst awaiting the establishment of wider international regulations for venereal-disease control, and that :
   (*a*) steps be taken for the publication and distribution by WHO of the revised edition of the individual treatment booklet early in 1950 ;
   (*b*) the revised edition of the WHO international venereal-disease treatment-centre list be made available as widely as possible and distributed in printed form to health administrations, port authorities, and other interested parties early in 1950.

(2) The draft text of the international health regulations for venereal-disease control be established as soon as possible for circulation to governments with emphasis on the following principles :

(*a*) free therapy for venereal diseases to be available in the treatment-centres of all member-states of WHO, regardless of the nationality of the patient ;

(*b*) infectious syphilis to be included among the diseases notifiable for statistical purposes to national health administrations by physicians as well as by medical institutions.

(3) Consideration be given to the establishment of a sub-committee consisting of four members to act as a technical consultative body for the application of the projected international health regulations for venereal-disease control when these come into force in 1951 or 1952.

(4) Venereal-disease control demonstration projects be established in major ports, as emphasized by the Health Assembly, especially in underdeveloped areas, and that such activities be given a high priority in the WHO venereal-disease programme, should funds from the Technical Assistance Programme of the United Nations be available in 1950 and 1951.

(5) Liaison be maintained between the Expert Committee on Venereal Infections and the Joint WHO/ILO Expert Committee on Hygiene of Seafarers established in 1949.

Treponematoses.—The general outlook prevailed in the previous two sessions of the Expert Committee that a major effort should be concentrated in the WHO venereal-disease programme on early infectious syphilis, prenatal syphilis, and infantile syphilis, using modern public health methods, and that work directed towards other venereal infections should be considered when representing a special public health problem in a geographical area, or where spread of disease from country to country was involved. It may appear desirable to give more detailed attention to the prevention of the late manifestations of syphilis. While the reduction of the damaging effects of late disease upon the central nervous system and the vascular tree constitutes an ultimate public-health objective, its accomplishment may best be attained through an attack upon early infections. The relative infrequency with which these complications are observed would appear to make it inadvisable at this time to divert available resources to a special consideration of the prevention and medical care of the effects of late syphilis. The original concept is, therefore, considered to remain sound, but several developments have occurred justifying a broader consideration of the entire group of treponematoses in addition to syphilis. These include the following considerations :

(1) *Technical.*

(*a*) The demonstrated uniform response of the various treponematoses of syphilis, yaws, pinta, and bejel to penicillin.

(*b*) The development of the treponemal antibody techniques of Turner and Nelson, permitting study of the biological and immunological relationship between the causative agent of the various treponematoses in man and animals.

(*c*) The recent support given to the identification of bejel as an endemic syphilitic disease.

(2) *Administrative.*

(*a*) The referring of treponematoses other than syphilis, notably bejel and yaws, by the Executive Board and the Health Assembly for consideration by the Expert Committee on Venereal Infections.

(*b*) The decision of the second Health Assembly to establish in 1950, under the expanded technical assistance programme of WHO, an Expert Committee on Treponematoses composed of nine members including three syphilis experts of the present Expert Committee on Venereal Infections.

It is recognized that treponemal diseases other than syphilis, particularly yaws, impose in themselves a serious social and economic burden upon countries where these diseases are endemic. Extensive endemic foci have been known to exist for decades in the tropical Americas, Africa, Asia, and in many islands of the Pacific. The multitude of names given to the various manifestations in these areas testify to the universality of the disease. The hypothesis of Hudson holds that the various treponematoses, syphilis included, are caused by the same organism in various parts of the world but exhibit different clinical and epidemiological patterns as a result of different environmental factors. The varieties encompass the sporadic syphilis of the temperate zones with its sexual transmission, tending to involve mucous surfaces with periods of latency and ability to invade the vascular tree and brain stem ; yaws, the disease of childhood in the tropics ; and the bejel of the desert. The last two are characterized by non-venereal transmission and surface lesions, but have few late sequelæ or congenital manifestations.

Mass application of penicillin in "eradication projects" has been carried out in limited areas in Africa (yaws) where communities enjoyed freedom from the disease over a period of months, prior to re-introduction of the disease; in small island groups, i.e., Pacific atolls (yaws) ; in a national Indian reservation in the U.S.A. (syphilis) and elsewhere. The rationale supporting the opinion that an eradication project on a larger scale be undertaken at this time is the favourable response to rapid penicillin-control techniques recently established in yaws, bejel, and pinta, offering an opportunity to reduce significantly the toll taken by treponematoses in areas where these diseases

are prevalent and where active work could be undertaken by health administrations. Available techniques lend themselves to mass application, because of simplicity of method, non-toxicity of the antibiotic, and the rapid epidemiological control of the disease which follows. A large-scale project should be carried out in a geographically delimited area with a high prevalence of disease, the mass attack being based on the use of repository penicillin preparations. The envisaged rural eradication project of syphilis and yaws in the island of Haiti and the Dominican Republic appears to fulfil these conditions, and the support given to this project by WHO, the Pan-American Sanitary Bureau, and the United Nations International Children's Emergency Fund, at the request of the Haitian and Dominican Republic governments, is noted with satisfaction.

Like yaws, bejel is a disease predominantly affecting children but without primary manifestations, although such have been produced by the inoculation of human volunteers. Recently support has been given to the identification of bejel as an endemic syphilitic disease, non-venereally acquired. There appears to be a high prevalence of this disease in endemic areas in the Middle East, which are currently being surveyed by WHO. The social and economic burden represented by its afflicted large population groups have been pointed out by the Iraq Health Administration to the first World Health Assembly, and the WHO Regional Committee for the Eastern Mediterranean recommended at its recent meeting that WHO and UNICEF should support suitable programmes for combating the disease in the region, including the establishment of a demonstration area in 1950, thus meeting the request of the government of Iraq.

The committee considers that the excellent bejel project for field and investigative activities, proposed by the Director-General and recommended by the Regional Committee for the Eastern Mediterranean, should go forward, and that attention of health administrations and institutions in the region be drawn to the supporting documentation for this project, with a view to further elucidation of the nature of this disease, the causative agent (*T. pallidum* of bejel) not having so far been isolated in the experimental animal.

Although it is recognized that syphilis, bejel, pinta, yaws (and certain natural treponematoses of animals) are epidemiological and perhaps clinical entities, the fundamental biological relationships within the larger group is still a matter of dispute. The resolution of this question may seem at first glance to be of limited importance, but considering the various syndromes from a world viewpoint, a knowledge of the basic relationship is necessary for an intelligent approach to control, for not only are there many practical ways in which such knowledge will be useful, but it will lift much uncertainty and irresolution from the minds of those who must make decisions regarding this large segment of human disease.

WHO can make a significant contribution, at little extra cost, to the ultimate definition of the nature of treponemal diseases in man, and their biological and immunological relationships, by utilizing the clinical and laboratory material available from field units and the organized participation of national laboratories in areas where treponematoses are prevalent.

Having carefully considered the relevant paragraphs of the report of the sub-committee on Serology and Laboratory Aspects, and the stimulating statement of Prof. T. Turner in this respect, the committee is convinced that this co-operative comparative study based on the Director-General's project represents an activity worthy of WHO's attention. It is recommended that:

(1) The syphilis/yaws project in the island of Haiti and the Dominican Republic go forward as soon as possible, and that:
   (*a*) the technique used be based on procaine penicillin G in oil with 2 per cent. aluminum monostearate;
   (*b*) at the present stage of planning, the establishment of a sound minimum administration and other control machinery be studied, to enable the health administration, with necessary outside assistance, to consolidate the public health gains obtained by the initial mass approach, these considerations including the study of measures for the prevention of reinfection;
   (*c*) the results obtained be studied in view of the importance of the application of such public health techniques to other areas where yaws and treponematoses are endemic.

(2) The bejel project in the Eastern Mediterranean area be activated early in 1950, and that:
   (*a*) a preliminary field study be undertaken at that time;
   (*b*) the pilot area be established in Iraq as soon as the hot season is over;
   (*c*) the co-operative international study of treponematoses go forward and a central scientific institution be selected to initiate and guide this study;

(3) The terms of reference of the Expert Committee on Treponematoses projected for 1950 be clarified, to avoid duplication of effort, or WHO give consideration to the merging in 1951 of the existing Expert Committee on Venereal Infections with the

Treponematoses Committee; appropriate study groups or sub-committees be constituted as required, and this question be considered further at the next meeting of the committee.

Anti-Venereal Drugs and Therapy

Availability of Penicillin.—The progress made and the co-operation achieved by WHO with the Economic Commissions of the United Nations in regard to the stimulation of penicillin production is noted by the committee. A study of the interim report on penicillin requirements and availability, based on the enquiry carried out by WHO at the suggestion of the original venereal disease committee, leads the committee to agree that this study is incomplete, and does not cover those areas where presumably the needs are greatest and where only limited data may be available for estimating the factual requirements. The committee considers that the study should be continued so that world-wide requirements of the drug can be further evaluated.

The activities in regard to the rehabilitation of the UNRRA penicillin plants and the recommendation for the establishment by WHO of an Expert Committee on Antibiotics have been noted. The committee wishes to reiterate its view that the limited availability of penicillin is a major restricting factor in the control of syphilis and related diseases in the world.

The work undertaken by WHO for the establishment of an international pharmacopoeia is welcome and the inclusion of basic anti-venereal-disease drugs in the International Pharmacopoeia will be of primary importance to health workers in many lands. It is suggested that the attention of the Expert Committee on Unification of Pharmacopoeias be drawn to the desirability of including, if possible, characteristics also of vehicles and water-repellant substances in identifying penicillin preparations—such as procaine penicillin G in oil with 2 per cent. aluminum monostearate. Only equal characteristics of all elements in repository preparations will enable truly comparative investigations to go forward. An indication of particle size and stability is particularly desirable. The committee is aware that this suggestion introduces an extension in principle of the work now being done by the Expert Committee on Pharmacopoeias, but believes it sufficiently important to warrant its being brought forward.

The committee considers that the following anti-venereal drugs should be included in the international pharmacopoeia:

Arsenoxides
Aureomycin
Neoarsphenamine
Sodium penicillin G
Procaine penicillin G
Streptomycin
Sulfadiazinum
Sulfaguanidinum
Sulfathiazolum

The Antibiotic Treatment of Syphilis and Related Diseases.—The situation outlined in previous reports of the committee in relation to gonorrhoea therapy and minor venereal diseases remains essentially the same, except in the case of lymphogranuloma venereum where initial experience indicates the beneficiary therapeutic value of aureomycin. Attention was also paid to the newer antibiotics introduced experimentally, namely, aureomycin and chloromycetin, which have been shown to possess treponemicidal activity. The presently accumulated knowledge does not indicate that they will play an immediate role in the control programme. The committee will carefully scrutinize the future development of these and similar substances with a view to their possible public-health value. An effective antibiotic orally administered might represent a development which would force alignment of the control mechanism in some geographic area.

The committee has reviewed in considerable detail the present status of antibiotic therapy, especially the use of penicillin alone in early syphilis, prenatal syphilis, and infantile syphilis, the important development represented by the introduction of reliable absorption-delaying preparations, and the results obtained with procaine penicillin G in oil and 2 per cent. aluminum monostearate. Penicillin in neurosyphilis and late manifestations was not considered at the present session. The participation in the discussions of the WHO Syphilis Study Commission to the U.S.A., the terms of reference of which included the study of venereal-disease control elements "with particular reference to penicillin in syphilis", was highly stimulating and permitted a wide international exchange of views and experience, emphasizing the current orientation on penicillin therapy in syphilis. Results of procaine penicillin with 2 per cent. aluminum monostearate in syphilis are only slowly accumulating outside the U.S.A., and the committee welcomed particularly the contribution made by the presentations, for the first time, of case-material from Europe, South East Asia, and South America.

True penicillin resistance has not been recorded in gonorrhoea (*in vivo*), syphilis, or other treponematoses, justifying the attitude that this non-toxic antibiotic should be used as widely as possible notwithstanding the recognized possibility that at some future date resistant strains of gonococci and treponemata may be observed.

The past six years of experience with penicillin therapy in syphilis have not established general agreement regarding dosage or the optimum time of treatment. Regardless of the opinions on time-dose relationships, and recognizing the continued application in Europe and elsewhere of adjuvant therapy (arsenicals and/or bismuth) after initial penicillin administration, the data now available has proved beyond doubt that so far penicillin is the best single antisyphilic agent for immediate treatment which has ever been used on a wide scale.

Newer Repository Penicillin Preparations.

Early Syphilis.—With the advent of respository penicillin preparations, further simplification of penicillin therapy has taken place. This has resulted from the ability of the newer absorption-delaying preparations of procaine penicillin with 2 per cent. aluminum monostearate to maintain demonstrable blood levels for prolonged periods. A single injection of 300,000 Oxford units of PAM *can* maintain an effective blood level for more than 96 hours.

There are under scrutiny by various investigators at this time several groups of patients treated for experimental purposes within one day, who received either a single injection, or a series of injections ranging from 300,000 to 600,000 Oxford units each. Treatment schemes are otherwise employed for a period of two to four weeks with injections at different time-intervals for a total dosage of 1·2, 2·4, and 4·8 million Oxford units of PAM.

The committee unanimously agreed that in the interests of public health, prompt penicillin therapy is essential in the treatment of all cases of early infectious syphilis. Although sufficient time has not yet passed since the advent of PAM to evaluate the ultimate outcome, studies followed carefully during the last two years indicate that results to date are better than with the penicillin preparations previously employed. It is remarkable that no completely acceptable instances of clinical central nervous system relapse in a patient receiving adequate penicillin therapy (aqueous, POB, PAM) in the early stages of infection appear to have occurred. This statement is valid for a small group of patients who have been under observation for approximately seven years and for a large group of patients who have had progressively shorter post-treatment observation. If this situation continues, the danger of syphilis of the central nervous system developing will largely have passed. The prolonged post-treatment follow-up which is presently necessary may be curtailed and a shorter routine adopted.

The manner in which data on treatment, re-treatment, clinical and serological relapses, sero-resistance, and reinfection in syphilis is recorded in penicillin case-material in relation to patient-percentage follow-up, at given intervals, over a period of time, differs from the organization of such material treated with arsenicals and/or bismuth in the past. This has made analysis of such material extremely difficult. An effort might be made to organize and analyse available material on series of patients treated with arsenic and/or bismuth, according to the requirements now exercised in penicillin-treated material. A review of suitable material should be presented to the committee at a subsequent meeting by a corresponding study-group of three committee members, with the above points in mind.

Prenatal and Infantile Syphilis.—The right time to treat infantile syphilis is prenatally. Women not studied for syphilis during pregnancy should be studied at the time of delivery or at the time the infant is presented for paediatric care.

Penicillin readily permeates the placenta from the maternal blood stream to the foetal tissues as early as the tenth week of gestation, as well as in the later months of pregnancy. Experience confirms that penicillin is superior to other treatment methods in the prevention of prenatal syphilis, the failure rates in terms of syphilitic infants remaining 1 to 4 per cent. when the mother is adequately diagnosed, treated, and followed-up during pregnancy. In syphilis in pregnancy, treated at a time when there is no evidence that damage to the foetus has occurred, there is no valid reason to expect infection in the infant, although the possibility, however remote, that a post-treatment relapse in the mother could lead to congenital damage of the fœtus should not be ignored. Some divergence of opinion exists as to the necessity for re-treatment during every subsequent pregnancy of the syphilitic woman. The possibility of the mother's being reinfected would dictate that every precaution should be taken to assure freedom from the disease in her subsequent offspring.

Treatment reactions during pregnancy have not proved to be serious and do not usually necessitate any modification of the treatment course. Currently available preparations of PAM appear to give satisfactory results with individual doses of 600,000 Oxford units, given once daily for total courses of 4·8 to 6 million units of penicillin. Treatment of the pregnant woman with PAM at 2- or 3-day intervals is still distinctly experimental. The optimum duration of the treatment course with penicillin for the syphilitic pregnant woman has not yet been determined.

In prenatally acquired syphilis (congenital syphilis in infants) the mortality rate is high (10 to 15 per

cent.). Great care should be taken with respect to supporting paediatric care during penicillin treatment, as therapeutic shock may be observed. Because of the frequent occurrence of pneumonia and other inter-current infections, it is considered desirable by some investigators not to modify the penicillin dosage.

A common practice has been to employ aqueous penicillin in early infantile syphilis by frequent injections in hospitalized cases (from 100,000 to 400,000 units per kg. bodyweight every 3 hours for 120 injections). In selected cases PAM has proved satisfactory in individual daily doses of 150,000 to 300,000 units per injection, although such experience is still limited.

The response of serologic tests, quantitatively followed, is in direct ratio to the age at which treatment is commenced. When treatment is started under the age of 6 months reversal to negativity approaches 100 per cent.

Other Public Health Aspects.—The advent of PAM has simplified therapy in syphilis and other treponematoses in which a foreshortened approach has been employed (yaws, pinta, bejel). The development of reliable non-toxic absorption-delaying preparations furnishes actual and potential epidemiological tools, previously not available. These are effective in severing the chain of infection in treponemal disease in man after initial application of even limited amounts of the antibiotic, administered over periods varying from hours to a few days. Their applicability to large population groups represents a major public-health development. Programmes designed to employ them on a larger scale should be organized as part of public-health activities in areas with a high prevalence of treponemal disease. Recognizing the epidemiological value of penicillin, the committee recommends that :

(1) Penicillin be used for *immediate* treatment of early infectious syphilis, prenatal syphilis, and infantile syphilis.

(2) Procaine penicillin G in oil with 2 per cent. aluminum monostearate (PAM) be used as widely as possible.

(3) A corresponding group composed of three members of the Expert Committee report at a subsequent meeting on a review of suitable case-material treated with (*a*) arsenicals and/or bismuth, and (*b*) penicillin preparations.

Serodiagnosis

Any sound venereal-disease activity is largely dependent upon the efficient conduct of serological tests for syphilis. The committee has previously pointed out the great lack of uniformity of procedure, technique, and manner of reporting results which has produced confusion and rendered valueless many studies of serology in syphilis and of the prevalence of the disease. The problem of biologically false-positive reactions and non-specific reactions in diseases other than syphilis has caused a wide search for further approaches to the problem. The most promising development in this regard is the introduction of the immobilizing antibody technique (Nelson and Turner), which has presented an opportunity for studying the wider aspects of immunological relationship between strains of *T. pallidum* and other treponematoses. The differentiation between what appear to be true and non-specific reagins employing this technique may in future prove of fundamental importance in the serodiagnosis of syphilis. Until the scientific evaluation of the merits of this development, now in its early stages, is made available, serological programmes must proceed along established lines, the treponemal antibody techniques remaining a research tool for the time being.

The committee has received and studied the report of the Sub-Committee on Serology and Laboratory Aspects. The committee approves fully the findings of this group, and the views and recommendations set forth. It further approves that this report be annexed to the report of the main committee with the following observations :

(1) The determination of the level of reactivity or sensitivity at which standard procedure is to be adjusted in order to convey the soundest information in terms of clinical syphilis is of major significance. This can only be established through the results of broad clinical and laboratory studies. The ground work for this type of activity is being laid at present in one area (U.S.A.) and similar studies in other parts of the world are necessary. A second consideration is the international exchange of information regarding the prevalence of syphilis based on serodiagnostic findings. This information would be of greater value if a universal test procedure could be employed, although it is recognized that a certain degree of non-specific findings are inescapable with the presently employed methods. Should a more reliable and informative standard test procedure, as well as a standardized antigen based on cardiolipin-lecithin be introduced on a national scale in one country, this may influence the orientation in other countries. WHO should watch such developments closely with a view to the establishment of an international antigen standard, and the eventual recommendation of a uniform test-method available to all countries where syphilis work is undertaken. This would remain the ultimate aim of WHO in this field. The many confusing factors which are present at this time would then be eliminated.

(2) The disproportionately high percentage of serologic findings among inhabitants in certain geographical

areas without concomitant proof of syphilitic manifestations remains. The contention is that test methods which are capable of producing a satisfactory standard of results in temperate climates fail to extend the same reliable service in population groups under tropical conditions. The impression is gaining strength that the rate of positivity is higher than is to be expected in relation to the frequency with which clinical manifestations of treponemal diseases are encountered; also, that the presence of other disease or infestations has not been noted with sufficient frequency to warrant the assumption that they are responsible for the serologic phenomenon. This situation may not necessarily constitute an indictment of present day serology. As the natural history of treponematoses becomes more clearly understood, the possibility of the tests themselves being capable of detecting changes attributed to the presence of syphilis-like organisms may be an eventuality, and may point towards the presence of sub-clinical treponemal infection which has escaped detection by all other methods. Looking ahead it will be necessary to gather more precise information on the subject through sampling operations in many tropical areas, including the study of inter-current infections, infestations, dietary and living habits of the population. With its far flung machinery WHO could contribute substantially to such a study.

(3) The desirability is recognized by the committee of developing a rapid serologic test for ambulatory use in mass screening procedures sufficiently sensitive and specific for the establishment of diagnosis and rapid application of therapy during short stays of field units in any one community in less developed areas with a high prevalence of syphilis. The difficulties in selecting such a test are clear from the foregoing, although various applicable procedures with recognized limitations are in use at this time, e.g., variations of the Chediak "blood-drop" technique, slide tests, filter-paper procedures, etc. The committee will watch with considerable interest the work of the Sub-Committee on Serology and Laboratory Aspects in this regard.

In approving the report of the first session of the Sub-Committee on Serology and Laboratory Aspects and the recommendations contained therein, the committee notes with satisfaction the progress made in the formulation of detailed plans for the International Serodiagnostic Laboratory Conference approved by the World Health Assembly and to be held in a major laboratory centre in 1951 or 1952.

The committee considers it important that WHO bring, as soon as possible, the programme outlined for the laboratory conference to the attention of national health administrations and laboratories with a view to preliminary registration of participants during the first half of 1950.

The committee points out that it is particularly desirable that:

(1) WHO bring to the attention of health administrations the necessity for maintaining a national reference laboratory for serodiagnosis of syphilis to control and guide the serodiagnostic performances of local laboratories.

(2) The Sub-Committee proceed as actively as possible with its programme for the establishment of an international antigen reference standard in close co-operation with the Expert Committee on Biological Standardization, that the possibility be studied for the recommendation of a uniform test procedure available to all countries, and that the possibility of establishing international reference centres making control sera and antigens available to national laboratories be explored.

Case-Finding and Health Education

A major effort should be directed towards case-finding in reservoirs of infection which perpetuate the transmission of disease in a population group. When control forces succeed in reducing the incidence and prevalence of syphilis and related diseases, the relative weight which must be allocated to the finding of the remaining individual cases increases. Available techniques for case-finding should be studied more closely in the light of present information as well as in relation to the characteristics of the particular area in question. Available case-finding mechanisms include:

(1) Contact investigation (epidemiological investigation) considered the most important single approach to finding cases of early syphilis.

(2) Public information and health education, employing a variety of techniques.

(3) "Screening" processes aiming at mass examination of individuals in occupational, economic, or other population segments (including prenatal and premarital serological testing, etc.).

There is evidence in several countries that there is a larger proportion of undiscovered females than there are males in the reservoir of venereal infections. This problem should receive special attention. The entire field of case-finding in syphilis and related diseases, the methods and techniques used, and the adaptation of these techniques to varying environments in different countries, would merit detailed consideration by the committee at a subsequent meeting.

It is recognized that in many parts of the world there is a great need to develop understanding and knowledge of measures to promote health and to prevent illness. The committee expresses its approval of the definitions, principles, and objectives of the WHO programme in the field of health education. It notes the excellence of the WHO statement in this regard and the suggested activities

relating to venereal-disease control. The health-education measures and the activities proposed for the WHO venereal-disease teams working with health administrations in the field should be implemented, and venereal-disease programme specialists should contribute to the development of an informed opinion with a view to overcoming cultural and social patterns which may hamper health programmes.

The committee wishes to emphasize the basic importance of the maintenance of the patient-physician relationship and the opportunities for the physician to develop a primary understanding in the patient of the nature of venereal diseases, their epidemiology, and the necessity for bringing possible contacts to treatment.

The committee wishes to point out the role which non-governmental and voluntary organizations can plan internationally, in each country and community, in furthering health-education programmes. Recognizing the significance of case-finding methods in the control of syphilis and related diseases, and that advice may be sought by the health administrations from the WHO on available mechanisms, their efficiency, and the applicability of techniques under varying circumstances, the committee recommends that :

> An enquiry into case-finding as applied to venereal-disease control be made with special reference to syphilis, and that material be collected from members of the Expert Committee, from health educators, and from other sources, as a basis for a report on this subject, to the fourth session of the committee.

WHO Syphilis Study Commission to the United States

The committee recalls the activities in the past of the New York Venereal Disease Commission to the Scandinavian countries (1936), the special commission appointed by the Minister of Health in England and Wales and the Secretary of State for Scotland to report on anti-venereal-disease measures in the Scandinavian countries and Holland (1938), and the report of the Anglo-American Caribbean Commission (1946), and notes the response of WHO to the original request of the United States government leading up to the establishment of the WHO Syphilis Study Commission, as set forth in detail by the Expert Committee. The activities of the Commission and the presence of its members at these meetings have been welcomed by the committee.

The committee holds the view that the interim report of the Commission represents a significant contribution. Valuable information on the United States venereal-disease control programme including data on penicillin in early syphilis, prenatal syphilis, and infantile syphilis has been collected and evaluated by the Commission, and has made possible a fuller consideration of this important question during the session.

The committee considers the establishment of *ad hoc* study commissions of an international character a valuable technique which WHO may wish to employ at the request of health administrations in the future, to carry out evaluation of health programmes of special national or international importance. The committee recommends that :

> The report of the WHO Syphilis Study Commission to the U.S.A. be published early in 1950 and made available to health administrations and other interested parties.

Relationships with other International Organizations and Committees within the Structure of WHO

The committee notes the co-operation established by WHO with projects and programmes for the combating of venereal diseases, notably with the United Nations International Children's Emergency Fund, the International Labour Organization, the International Refugee Organization, and the International Union against Venereal Disease (the last-named being the only non-governmental international anti-venereal-disease organization with whom WHO has official relationship). Specific reference has been made elsewhere in this report to projects in co-operation with the United Nations International Children's Emergency Fund and the International Labour Organization. As regards the International Union against Venereal Diseases, the committee notes the resolutions of the General Assembly in Rome earlier in 1949, and expresses the hope that the Union will continue to study venereal-disease projects of important social significance which are suitable for international action, and that the activities of the organization will go forward with emphasis on positive health education, and other basic social problems related to venereal-disease control.

Within the framework of WHO, the committee notes the recommendations made by the Expert Committees on Mental Health, Biological Standardization, and Unification of Pharmacopœias, as well as by the Joint WHO/ILO Expert Committee on Hygiene of Seafarers. Consideration has been given by the committee to the respective items under health education, serology in syphilis, anti-venereal drugs, international health regulations, etc. Specific reference has been made to the relationship of the main committee with the Sub-Committee on

Serology and Laboratory Aspects, and with the WHO Syphilis Study Commission.

REFERENCES

(1936). *Amer J. Syph.*, **20,** Part 2 (July). Control of Syphilis and Gonorrhoea in the Scandinavian Countries and Great Britain. A Report of the New York City Commission to Investigate the Prevention and Control of Syphilis and Gonorrhoea in the Scandinavian Countries and in Great Britain.

Harrison, L. W. (1938). "Anti-venereal Measures in certain Scandinavian Countries and Holland". Ministry of Health Report No. 83.

Wenger, O. C. (1946). "Caribbean Medical Center, Port of Spain, Trinidad (1943-45)". Caribbean Commission, Washington, D.C., U.S.A.

TENTH INTERNATIONAL CONGRESS OF DERMATOLOGY

Preliminary Notice

The Tenth International Congress of Dermatology will be held in London during the summer of 1952, under the presidency of Sir Archibald Gray.

A preliminary programme will be prepared during the current year.

As a result of the disruption produced by the last war, the addresses of the secretaries of certain Dermatological Societies are not available, so that all those interested are asked to communicate with me at the Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London, W.C.2.

GORDON B. MITCHELL-HEGGS, M.D.,
General Secretary.